Anal. Calcd for $C_9H_{19}N_3O_2$: C, 53.71; H, 9.52; N, 20.88. Found: C, 53.97; H, 9.71; N, 21.06.

Pyrolysis of Trimethylamine-β-phenylcarbamoylpropionimide (1d).—Pyrolysis of the aminimide (5.22 g) at 200–220° gave a liquid which distilled and a solid residue. The liquid, based upon chromatographic analysis using a silicone rubber W98 column, consisted of aniline (0.5 g), *N*-methylaniline (0.16 g), and *N*-dimethylaminosuccinimide (**3**) (0.18 g).

The residue upon chromatography using a silica gel column and ethyl acetate as the eluting solvent gave *N*-phenylsuccinimide (1.08 g), mp 152.5–154.5° (lit.[12] mp 155°), and 1,2,3,4,5,6-hexahydro-3-phenyl-2,4-dioxopyrimidine (**4b**) (0.34 g), mp 233.5° (lit.[13] mp 231–234°). Identification was made by comparison with authentic samples.

Pyrolysis of Trimethylamine-β-ethylcarbamoylpropionimide (1e).—Decomposition of the aminimide (5.02 g) at 200–220° gave a dark solid (3.51 g) which upon vacuum sublimation at 120° (16 mm) gave a white solid (3.34 g). Analysis by gas chromatography at 220° using a silicone rubber W98 column showed two compounds in a 12:1 ratio. The first component was identified by its migration as *N*-ethylsuccinimide. The second component was isolated by recrystallizing the mixture from ethanol and was identified as 1,2,3,4,5,6-hexahydro-3-ethyl-2,4-dioxopyrimidine (**4c**) by comparison with a sample synthesized from *N*-ethylsuccinamide, yield 2.89 g, mp 113–114.5°.

1,2,3,4,5,6-Hexahydro-3-ethyl-2,4-dioxopyrimidine (4c).—A solution of *N*-ethylsuccinamide (3.3 g) and lead tetraacetate (10.5 g) in dimethylformamide (30 ml) was heated with stirring at 60–70°. Removal of the dimethylformamide gave a solid which was extracted with ether. Removal of the ether followed by recrystallization from ethanol gave white crystals melting at 113.4–114.5°: yield 0.94 g; ir (Nujol) 3285, 3120 (NH), 1720, 1650 cm^{-1} (CO); nmr ($CDCl_3$) δ 7.32 (s, 1, NH), 3.80 (q, 2, NCH_2CH_3), 3.40 (t, 2, CH_2NH), 2.68 (t, 2, CH_2CO), 1.13 (t, 3, CH_3); mol wt 142 (mass spectrum).

Anal. Calcd for $C_6H_{10}N_2O_2$: C, 50.69; H, 7.09; N, 19.71. Found: C, 50.89; H, 7.24; N, 19.92.

***N,N,N*-Trimethyl-*N*-(*N'*-succinimido)ammonium Methyl Sulfate.**—A solution of *N*-dimethylaminosuccinimide (20.0 g) and methyl sulfate (20.2 g) in benzene (400 ml) was refluxed for 24 hr. The solid (12.4 g) formed upon cooling was filtered. The filtrate upon refluxing for an additional 24 hr gave more of the product (16.6 g). Recrystallization of the combined solids from methanol–ether gave white crystals melting at 147.5–149.5°: yield 21.0 g; ir (Nujol) 1895, 1740 (cm^{-1} (CO); nmr (D_2O) δ 4.20 [s, 9, $N(CH_3)_3$], 3.90 (s, 3, CH_3OSO_3), 3.12 (s, 4, CH_2CH_2).

Anal. Calcd for $C_8H_{16}N_2O_6S$: C, 35.81; H, 6.01; N, 10.44. Found: C, 35.80; H, 6.07; N, 10.24.

Reaction of *N,N,N*-Trimethyl-*N*-(*N'*-succinimido)ammonium Methyl Sulfate with Barium Hydroxide.—A solution of the methyl sulfate (5.36 g) and barium hydroxide octahydrate (6.31 g) in water (100 ml) was heated in a sealed flask on a steam bath for 3 weeks. The solution was filtered periodically to remove the barium sulfate. After this period the theoretical amount of barium sulfate was isolated. The resulting solution was saturated with carbon dioxide, filtered, and concentrated to dryness. The resulting product (3.51 g) was a glassy material which was extremely hygroscopic and could not be crystallized. A portion (1.41 g) of this material, when treated in water (50 ml) with 0.0650 *N* hydriodic acid (7.31 ml) gave after removal of the solvent a solid which melted at 229–230° after one recrystallization from methanol, yield 1.1 g. The ir spectrum was identical with that of 1,1,1-trimethylhydrazinium iodide and a mixture melting point was not depressed.

Registry No.—**1a**, 39267-13-5; **1b**, 39267-14-6; **1c**, 39267-15-7; **1d**, 39267-16-8; **1e**, 39267-17-9; **3**, 10574-06-8; **4c**, 39267-19-1; *N,N*-dimethylaminosuccinamic acid, 1596-84-5; succinic anhydride, 108-30-5; 1,1-dimethylhydrazine, 57-14-7; 1,1,1-trimethyl-2-(β-carboxypropionyl)hydrazinium iodide, 39267-21-5; methyl iodide, 74-88-4; methyl β-succinimidopropionate, 39267-22-6; methyl β-aminopropionate hydrochloride, 3196-73-4; succinyl chloride, 543-20-4; methyl *N,N*-dimethylaminosuccinamate hydrochloride, 39267-24-8; methyl *N,N*-dimethylaminosuccinamate, 28402-64-4; β-carbomethoxypropionyl, 1490-25-1; trimethylamine, 75-50-3; 1,1,1-trimethyl-2-β-carbomethoxypropionylhydrazinium iodide, 39267-27-1; 1,1,1-trimethyl-2-β-carbomethoxypropionylhydrazinium chloride, 39477-74-2; methyl chloride, 74-87-3; phenyl isocyanate, 103-71-9; *N*-ethylsuccinimide, 2314-78-5; *N,N,N*-trimethyl-*N*-(*N'*-succinamido)ammonium methyl sulfate, 39267-28-2; barium hydroxide, 12230-71-6; 1,1,1-trimethylhydrazinium iodide, 3288-80-0.

---

[12] G. Koller, *Ber.*, **37**, 1598 (1904).

[13] S. Hoogewerff and W. A. VanDorp, *Recl. Trav. Chim. Pays-Bas*, **9**, 33 (1890).

3-Substituted Oxetanes

J. A. WOJTOWICZ*[1] AND R. J. POLAK

Research Center, Olin Corporation, New Haven, Connecticut 06504

Received February 23, 1972

3-Allyloxyoxetane was rearranged to 3-propenoxyoxetane in 85–90% yield. The *t*-BuOK-catalyzed isomerization was essentially stereospecific, yielding 96% cis isomer. The propenyl ether was cleaved by acid hydrolysis to produce 3-oxetanol in 84% yield. Esterification of oxetanol with tosyl chloride gives crystalline oxetyl tosylate in 90–95% yield. Oxetanone is formed either by mild oxidation of oxetanol with chromic oxide–pyridine complex or by heating oxetyl tosylate in dimethyl sulfoxide. Heating oxetyl tosylate above 150° with alkali halides in triethylene glycol gave 75–85% yields of 3-halo oxetanes as overhead product in about 95% purity. A lower yield (10–20%) of 3-chlorooxetane was obtained when 3-oxetanol was treated with thionyl chloride. Reaction of iodooxetane with diethylamine at 200° gave 3-dimethylaminooxetane. Oxetyl acetate was prepared in 84% yield by transesterification of oxetanol with allyl acetate. Transesterification of oxetanol with ethyl acrylate gave a low yield of oxetyl acrylate; the main product was ethyl 3-(3'-oxetoxy)propionate. The acetate and acrylate esters were also prepared by acylation of oxetanol. Attempts to prepare oxetene by dehydrotosylation of oxetyl tosylate, dehydroacetoxylation of oxetyl acetate, or dehydrohalogenation of chloro- and iodooxetanes were unsuccessful.

The synthesis of 3-allyloxyoxetane[2] afforded an intermediate from which a variety of monosubstituted oxetanes could be prepared.

The work which is presented in this article deals with the isomerization of allyloxyoxetane to propenoxyoxetane followed by cleavage of the propenyl ether to 3-oxetanol[3] and conversion of the latter to halo oxetanes[4] and other new oxetanes.

---

[1] Address correspondence to this author.

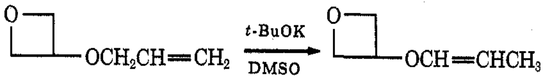
[2] J. A. Wojtowicz, R. J. Polak, and J. A. Zaslowsky, *J. Org. Chem.*, **36**, 2232 (1971).

[3] A. E. Ardis and J. A. Wojtowicz, U. S. Patent 3,446,819 (1969).

[4] S. L. Clark, R. J. Polak, and J. A. Wojtowicz, U. S. Patent 3,517,030 (1970).

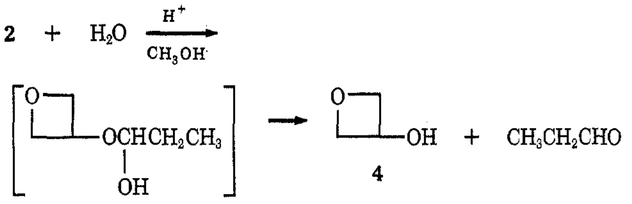
Discussion

Price and Snyder[5] have shown that rearrangement of allyl to propenyl ethers catalyzed by *t*-BuOK in dimethyl sulfoxide is rapid, essentially stereospecific (99% cis isomer), and virtually quantitative. Utilizing this technique, 3-allyloxyoxetane was isomerized to 3-propenoxyoxetane in 85–90% yield. The high conversion (95%) achieved is due to the near-theoretical equilibrium afforded by *t*-BuOK. The product **2** consisted of 96% cis and 4% trans isomer.



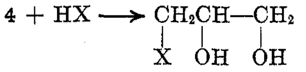
1 2

Initial attempts to prepare 3-oxetanol from 3-propenoxyoxetane by cleaving the propenyl ether *via* hydroxylation with alkaline permanganate were not successful owing to attack of the oxetane ring by $KMnO_4$. The propenyl ether, however, was successfully cleaved under mild conditions by acid-catalyzed hydrolysis to 3-oxetanol.



3

3-Oxetanol readily reacts with anhydrous acids (HCl and HBr), forming 3-halopropanediols in high yields. In contrast, treatment of **4** with anhydrous HF resulted



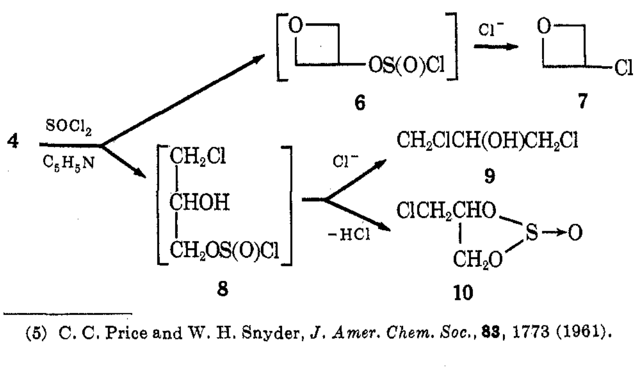
$$4 + HX \longrightarrow \underset{X}{CH_2}\underset{OH}{CH}\text{—}\underset{OH}{CH_2}$$

5

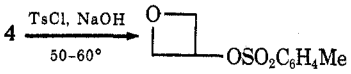
in polymerization. Heating oxetanol in dilute aqueous sulfuric acid gave glycerin in good yield.

Oxetanol slowly polymerizes on standing (under the influence of certain impurities), forming a low molecular weight (1400–1800), white, amorphous solid (mp 125–135°) which is insoluble in monomer. Nmr and infrared examination are consistent with the following structure for the water-soluble polymer: $[-CH_2CH(OH)CH_2O-]_x$.

Treatment of 3-oxetanol with thionyl chloride in pyridine gave low yields of chlorooxetane (10–20%). The main side reaction was ring opening leading to formation of 1,3-dichloropropanol and the cyclic sulfite ester of 3-chloropropanediol. The latter consisted of approximately equal amounts of cis and trans isomers. Products **9** and **10** most probably are formed from **8**; the latter arises from oxetane ring opening by $SOCl_2$. Reaction of 3-chloropropanediol with $SOCl_2$ in pyridine also gave **10** but no **9**; however, under more vigorous conditions[6] dichloropropanols and trichloropropane can also be formed.

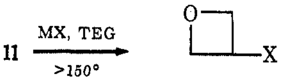


The tosylate route[7] provided a convenient method for preparing halo oxetanes. Oxetyl tosylate yields of 90–95% were consistently obtained by reaction of oxetanol with *p*-toluenesulfonyl chloride (tosyl chloride) in the presence of aqueous sodium hydroxide. Side reactions appear to give small amounts of ring-opening products.



11

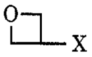
Oxetyl tosylate was converted to 3-halo oxetanes by displacement with alkali metal halides in triethylene glycol (TEG).[8] Yields of 3-halo oxetanes were in the range of 60–85%. The data are presented in Table I. The crude products assayed 95% or higher. In the absence of solvent a lower yield (65% compared to 83%) of 3-fluorooxetane was obtained, a higher temperature (200°) was required to initiate reaction, and a much lower reaction rate was observed.



12, X = F
13, X = Br
14, X = I

Table I

Preparation of Halo Oxetanes



X	Oxetyl tosylate g	Oxetyl tosylate Mol	Triethylene glycol, ml	Alkali halide g	Alkali halide Mol	Halo Oxetane g	Halo Oxetane Mol	Yield, %
F	456	2.00	450	465	8.00 (KF)	126	1.66	83[a]
Cl	372	1.63	375[b]	75	1.81 (LiCl)	116	1.25	77
Br	57	0.25	80	36	0.30 (KBr)	20	0.15	60
I	279	1.22	400	220	1.33 (KI)	191	1.04	85

[a] A lower yield of 65% was obtained in the absence of solvent at 200–225°. [b] Using diethylene glycol as solvent the crude product contained dioxane which was extremely difficult to remove by distillation owing to the closeness of its boiling point (101.5°) to that of 3-chlorooxetane (104°).

In the preparation of 3-iodooxetane the main impurities in the crude product were allyl alcohol and iodine. These impurities probably arise from reaction of iodooxetane with HI (from thermal decomposition of iodooxetane) to form 2,3-diiodopropanol, which can thermally decompose. The addition of iodine to allyl alcohol is known to be reversible.[9]

Bigot[10] reportedly prepared "β-epichlorohydrin"

---

[5] C. C. Price and W. H. Snyder, *J. Amer. Chem. Soc.*, **83**, 1773 (1961).

[6] P. B. D. DeLaMare, W. Klyne, D. J. Millan, J. G. Pritchard, and D. Watson, *J. Chem. Soc.*, 1813 (1956).

[7] G. V. D. Tiers, H. A. Brown, and T. S. Reid, *J. Amer. Chem. Soc.*, **75**, 5978 (1953).

[8] An alternate preparation of 3-fluorooxetane which involves dehydrohalogenation of 3-halo-2-fluoropropanols will be discussed in a succeeding publication.

[9] B. P. Caldwell and F. A. Pointkowski, *J. Amer. Chem. Soc.*, **56**, 2086 (1934).

[10] A. Bigot, *Ann. Chim. (Paris)*, **22**, 433 (1891).

(3-chlorooxetane) by treating 3-iodo-2-chloropropanol with base. However, it was subsequently shown[11] that the product isolated by Bigot was in fact 2-chloroallyl alcohol.

The isolation of "β-epiiodohydrin" (3-iodooxetane) from dehydrohalogenation of the isomeric allyl alcohol chloro iodides was also claimed by Bigot. His reported boiling point (172–174°) is much too high. The inertness of his product to aqueous KOH at 100° is suggestive of a vinyl type halogen, as would be present in 2-iodoallyl alcohol. The latter could form from dehydrohalogenation of 2,3-diiodopropanol, a not unexpected by-product in the chloroiodination of allyl alcohol. The iodine analysis reported is correct for the suggested compound.

3-Halo oxetanes, like the isomeric epihalohydrins, are colorless liquids possessing ethereal odors and except for fluorooxetane (which is freely miscible with water) are essentially water insoluble. They possess lower boiling points (owing to the presence of secondary halogen atoms) and higher densities (owing to their compact structure) than the epihalohydrins. The physical properties of the halo oxetanes are given in Table II.

Table II

Physical Properties of Halo Oxetanes[a]

Compd	Bp, °C	d_4 (temp, °C)	n^{20}_D	Ir bands[e] Oxetane ring[d]	Ir bands[e] C–X stretch
$\mathrm{FCHCH_2OCH_2}$	67	1.109 (26)	1.3729	10.32	9.22
$\mathrm{ClCHCH_2OCH_2}$	104	1.197 (25)	1.4418	10.28	15.30
$\mathrm{BrCHCH_2OCH_2}$	125–126[b]	1.773 (29)	1.4863	10.31	18.30
$\mathrm{ICHCH_2OCH_2}$	159[c]	2.089 (28)	1.5631	10.32	20.60

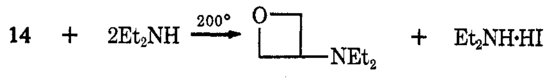
[a] Satisfactory analyses (±0.3% in C, H, and halogen) were obtained for all compounds in the table. [b] 66° (97 Torr). [c] 78° (47 Torr) and 40° (7 Torr). [d] Asymmetric C–O–C stretch. [e] Wavelengths are in microns, ±0.05 μ.

Fluorooxetane was the only halo oxetane which displayed a first-order nmr spectrum. In the case of chlorooxetane the complete five-spin AA'BB'C spectrum (at 90 MHz) occurred within 0.53 ppm. Although resolution was quite good, the spectrum could not be exactly interpreted without computer analysis.

The infrared absorption bands (CH_2 wag, ~8 μ; symmetric and asymmetric C–O–C stretch, ~9.8 and ~10.3 μ; and CH_2 rock, 11–13 μ) of 3-halo oxetanes shift toward higher wavelengths with increasing size of the halogen substituent. 3-Fluorooxetane shows some exceptions to this trend. It also exhibits a strong C–H deformation band at 7.3 μ. This band appears as a very weak absorption at 7.5–7.6 μ in the other halo oxetanes.

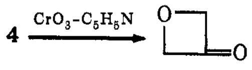
The facile reaction of halo oxetanes with anhydrous acids yields 2,3-dihalopropanols; this is exemplified by the reaction of **7** with HCl to give $CH_2ClCHClCH_2OH$.

Iodooxetane did not react appreciably with diethylamine below 200°. At 200° diethylaminooxetane was obtained in about 20% yield. The low yield is caused by ring opening initiated by the coproduct $Et_2NH \cdot HI$. Reaction of the latter with **15** initially gives $HOCH_2CH(NEt_2)CH_2I$, which reacts further with Et_2NH to form $HOCH_2CH(NEt_2)CH_2NEt_2$. Reaction of **14** with $Et_2NH \cdot HI$ yields $HOCH_2CHICH_2I$, which can react with Et_2NH or thermally decompose to give allyl alcohol and iodine.



15

Mild oxidation of oxetanol with chromic oxide–pyridine[12] complex gave 3-oxetanone in 55% yield.



16

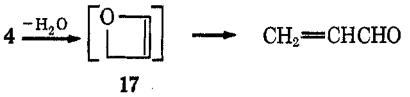
Use of permanganate, dichromate, or Oppenauer oxidation was not successful. Reaction of oxetyl tosylate with dimethyl sulfoxide in the presence of tri-*n*-butylamine gave a 33% yield of oxetanone. The major anticipated product of this reaction, oxetene, was not obtained. Sulfonate esters of secondary alcohols normally yield olefins on heating in dimethyl sulfoxide,[13a] whereas primary tosylates gave high yields of aldehydes.[13b]

Oxetanone exhibits carbonyl absorption at 5.47 μ in the infrared region, indicating a highly strained ring. It is unstable in the presence of base. Oxetanone slowly polymerized on standing, giving a highly viscous material which showed both carbonyl and ether absorption in the infrared and is indicative of polyoxetanone, $[-CH_2C(O)CH_2O-]_x$.

Oxetanone was first prepared[14] (in low yield) by reaction of chloroacetyl chloride with diazomethane followed by treatment with K_2CO_3 and isolation as the dinitrophenylhydrazone, mp 152–155°. Berezin[15] prepared oxetanone (40% yield) by hydroxylation of methyleneoxetane to 3-hydroxymethyl-3-oxetanol followed by cleavage of the glycol. Reduction of **16** in aqueous solution with ruthenium and hydrogen yields **4**.

Although substituted oxetenes have been reported, their structures have not been confirmed. Several attempts were made to prepare the parent compound, oxetene; none were successful. As mentioned earlier, thermal dehydrotosylation of oxetyl tosylate in DMSO did not yield oxetene. Likewise, thermal and chemical dehydroacetoxylation did not lead to oxetene formation. Dehydrohalogenation of chloro and iodo oxetanes gave several products which are indicative of ring fragmentation as well as rearrangement of the desired oxetene (to acrolein).

Dehydration of oxetanol over alumina at 400° gave a crude reaction product which contained water, formaldehyde, acetaldehyde, and acrolein. The latter probably forms by rearrangement of the desired oxetene.



17

---

[11] W. E. Noland and B. N. Bastian, *J. Amer. Chem. Soc.*, **77**, 3395 (1955).

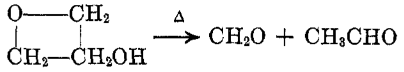
[12] G. I. Poos, G. E. Arth, R. E. Beyler, and L. H. Sarett, *J. Amer. Chem. Soc.*, **75**, 422 (1953). J. C. Collins, W. W. Hess, and F. J. Frank, *Tetrahedron Lett.*, 3363 (1968).

[13] (a) H. R. Nace, *Chem. Ind. (London)*, 1626 (1958); (b) N. Kornblum, W. J. Jones, and G. J. Anderson, *J. Amer. Chem. Soc.*, **81**, 4113 (1959).

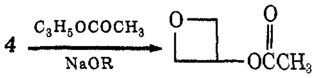
[14] J. R. Marshall and J. Walker, *J. Chem. Soc.*, 467 (1952).

[15] G. H. Berezin, U. S. Patents 3,297,719 (Jan 1967) and 3,449,369 (June 1969).

The formation of formaldehyde and acetaldehyde is indicative of thermolytic ring cleavage.

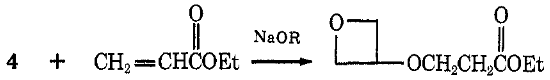


Transesterification of oxetanol with allyl acetate provided oxetyl acetate in 83% yield.



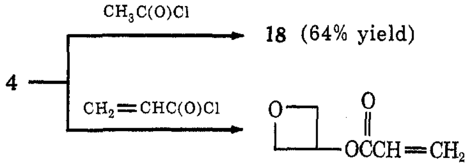
18

Using ethyl acrylate, a low yield (6%) of oxetyl acrylate was obtained. In addition to polymer formation the main by-product (16% yield) was derived from addition of oxetanol to the double bond of ethyl acrylate.



19

Acylation of oxetanol with acrylyl chloride provided a more satisfactory method for preparing oxetylacrylate; **18** was similarly prepared by treatment of **4** with acetyl chloride in the presence of pyridine.



20

Experimental Section

Materials.—3-Allyloxyoxetane was prepared from allyl alcohol and assayed >98%. Other chemicals were commercially available reagent grade.

Analyses.—Gas chromatographic (gc) analyses were conducted using an Aerograph A-90-P manual temperature programmer using 0.25-in. columns. Carrier gas flow was 40 cc/min at 40 psig. Most analyses were carried out using a 5-ft silicone SF-96 column (20% on 80–100 mesh Chromosorb), a 5-ft Igepal column (15% on 80–100 mesh Chromosorb W), or a 3-ft Carbowax 20M Column (5% on 80–100 mesh Chromosorb W). Quantitative analyses were performed using standards of known composition.

Infrared spectra of liquid samples (neat) or solid samples (as Nujol mulls) between salt plates were recorded with a Perkin-Elmer Infracord Model 137. Some spectra were also recorded with a Perkin-Elmer Model 21 spectrometer. Absorption bands due only to the main functional groups in the molecule are given. Complete spectra will be published in the near future by Sadtler.

^{1}H and ^{19}F nmr spectra were obtained with a Varian A-60 spectrometer. Some proton spectra were also recorded at 90 MHz with a Bruker spectrometer. Tetramethylsilane and $CFCl_3$ were used as internal references.

3-Propenoxyoxetane.—Dimethyl sulfoxide (700 g) and 3-allyloxyoxetane (456 g, 4.0 mol) in a 2-l. three-neck flask were treated (with stirring) with potassium *tert*-butoxide (51 g, 0.46 mol) over a 10-min period. The temperature rose to about 50° after 30 min. Infrared (disappearance of terminal methylene bands at 1.633 and 2.113 μ) and nmr indicated almost complete conversion of allyloxyoxetane. Gc analysis (140°, Igepal column) showed a conversion of 95% as well as the presence of *tert*-butyl alcohol. The latter results from the equilibrium $CH_3S(O)CH_3 + t\text{-BuOK} \rightleftarrows CH_3S(O)CH_2K + t\text{-BuOH}$. Filtration followed by distillation through a 24-in. Berl saddles packed column afforded propenoxyoxetane (388 g, 3.4 mol, 85% yield): bp 73–77° (50 mm); d_4^{25} 0.9752; n^{20}_D 1.4458; ir 3.27 (cis C–H stretch), 5.97 (C=C), 7.25 and 7.35 (methyl C–H deformation), 8.86 (COC), 10.23 (oxetane ring), and 13.7 μ (cis-propenyl C–H out of plane bending); nmr (60 MHz, $CDCl_3$) (the product is mainly the cis isomer containing about 4% trans isomer)—the propenyl portion of the molecule gave signals at δ_B 1.62 (CH_3), δ_A ~4.5 ppm (=CHC–), and δ_C 5.83 ppm (OCH=); the coupling constants are $J_{AB} \cong 6.5$, $J_{AC} \cong 6.3$, and $J_{BC} \cong 1.7$ Hz; the oxetane ring protons gave a complex uninterpretable multiplet between δ 4.5 and 4.9 ppm. The observed spectrum is actually composed of two five-spin systems (AA′BB′C and A_3MX) which involves over 500 theoretical transitions.

Anal. Calcd for $C_6H_{10}O_2$: C, 63.1; H, 8.83. Found: C, 63.2; H, 8.87.

3-Oxetanol—3-Propenoxyoxetane (136 g, 1.19 mol), water (132 g), methanol (97 g), and 98% H_2SO_4 (0.2 ml) were stirred at room temperature. Methanol was used as cosolvent, since propenoxyoxetane is soluble in water to less than 1% in contrast to allyloxyoxetane, which has a solubility of 15% in water at room temperature. The hydrolysis was conducted at room temperature because of the lability of the oxetane ring in acid media. Under the moderate temperature conditions employed the rate of hydrolysis was quite slow, requiring 5 days to attain 85% conversion (Analysis by gc: 170°, Igepal column). A faster reaction rate could probably be achieved by chemically tying up the propionaldehyde as it formed by means of the oxime or other derivative. The mixture was neutralized with NaOH and stripped in a rotary evaporator at 50° under water aspirator vacuum. The residue was distilled through a 24-in. spinning band column giving 3-oxetanol (62.7 g, 0.85 mol, 84% corrected yield): bp 72–73° (9 mm); d_4^{28} 1.125; n^{20}_D 1.4384; ir 2.94 (OH) and 10.36 μ (oxetane ring); nmr (60 MHz, $CDCl_3$) (a first-order spectrum was not obtained)—the oxetane ring protons gave a complex uninterpretable pattern between δ 4.3 and 5.0 ppm, the hydroxyl proton gave a doublet centered at δ 3.37 ppm (J_{HCOH} = 4 Hz).

Anal. Calcd for $C_3H_6O_2$: C, 48.6; H, 8.2. Found: C, 48.5; H, 8.1.

Oxetanol (neat) was treated with anhydrous HCl and HBr at 0°. The pure products were isolated by gc (150–200°, Carbowax column) and identified as 3-chloro-1,2-propanediol and 3-bromo-1,2-propanediol by their ir spectra. Yields were in the neighborhood of 90%.

Oxetanol (1 ml) was refluxed in 1 *N* H_2SO_4 (5 ml) for 30 min. The reaction mixture was neutralized, evaporated, extracted with isopropyl alcohol, and stripped of solvent. Gc and ir showed the product to be about 90% glycerin.

Oxetyl Tosylate.—The reactor was a three-neck, round bottom, 3-l. flask fitted with stirrer, thermometer, and addition funnel. A 20% aqueous caustic solution [NaOH 240 g (6.0 mol), H_2O 1200 ml] was added dropwise to a well-stirred mixture of oxetanol (400 g, 5.40 mol), water (1050 ml), and tosyl chloride (1086 g, 5.70 mol) at 50–55°. Stirring was continued for 1 hr after addition of base; the reaction mixture was neutral to phenolphthalein. After cooling (to room temperature), benzene (1 l.) was added to dissolve the tosylate, the layers were separated, and the aqueous layer was extracted twice with 100 ml of benzene. The combined benzene extracts were washed three times with concentrated NH_4OH to remove unreacted tosyl chloride and then with water to remove NH_4OH. The benzene was removed under vacuum. The solid product was ground with a mortar and pestle and freed of traces of solvent under vacuum. The crude tosylate [1109 g (4.87 mol), 90% yield] melted at 84–87°; after recrystallization from hexane it melted sharply at 88.5–89.0°. The crude product was sufficiently pure for further synthetic work, ir 7.3–7.4 and 8.4–8.5 (SO_2) and10.32 and 10.59 μ (oxetane ring).

Anal. Calcd for $C_{10}H_{12}O_4S$: C, 52.6; H, 5.3; S, 14.1. Found: C, 52.8; H, 5.3; S, 14.1.

3-Fluorooxetane.—Oxetyl tosylate (456 g, 2.00 mol), triethylene glycol (450 ml), and dry KF (465 g, 8.00 mol) were charged into a three-neck, 2-l. flask fitted with stirrer, thermometer, distillation head, and receiver (cooled with Dry Ice). A Dry Ice cooled trap was employed between the receiver and vacuum pump. The system, under reduced pressure (200 Torr), was heated in an oil bath and maintained a 160–170° until the distillation rate was noticeably reduced and then the temperature was slowly raised to 200° to remove the last traces of product. Some difficulty was encountered owing to foaming; this was alleviated by increasing the stirring rate, increasing the pressure slightly, and lowering the temperature or adding more solvent. The product, fluorooxetane [126 (1.66 mol), 83% yield], was more than 95% pure by gc (100°, silicone column). Redistillation through a 35-cm glass helices packed column gave pure fluorooxetane: bp 67° (760 mm); d_4^{26} 1.109; $n^{20}\mathrm{D}$ 1.3729; ir 9.22 (C–F) and 10.32 μ (oxetane ring); nmr ($CDCl_3$) two doublets (four methylene protons) centered at 268 Hz (δ_A 4.65 ppm) and two pentets (one methine proton) centered at 279 Hz (δ_B 5.38 ppm), $J_{AB} = 5$, $J_{AF} = 22.5$, and $J_{BF} = 56$ Hz (from ^{19}F spectrum $J_{AF} = 23.6$ and $J_{BF} = 58$ Hz).

Anal. Calcd for C_3H_5OF: C, 47.4; H, 6.63; F, 25.0. Found: C, 47.3; H, 6.59; F, 25.2.

Data on the preparation of other halo oxetanes are given in Table I. The physical properties of halo oxetanes are shown in Table II.

3-Chlorooxetane (from 3-Oxetanol and Thionyl Chloride.)—Thionyl chloride (0.22 ml, 3.0 mmol) was added dropwise to oxetanol (0.20 ml, 3.0 mmol) dissolved in pyridine (0.80 ml). An exothermic reaction occurred, yielding a brown precipitate and a dark brown supernatant liquid. Gc (125°, silicone column) showed complete consumption of oxetanol and the appearance of four new peaks at retention times of 2, 5, 9, and 11 min. Peaks 1 and 2 were identified (after trapping) as 3-chlorooxetane (~15% yield) and 1,3-dichloropropanol by their ir spectra. Peaks 3 and 4 were identified by ir (sulfite 8.35, C–Cl 13.5 μ) and nmr as the cis and trans isomers (~50:50) of the cyclic sulfite ester of 3-chloro-1,2-propanediol. This was substantiated by treating 3-chloro-1,2-propanediol with $SOCl_2$ in pyridine; the cis and trans isomers of the sulfite ester were formed but no dichloropropanol. No chlorooxetane was obtained from oxetanol when dioxane, β-picololine, or tri-n-butylamine were substituted for pyridine or with PCl_3 in place of $SOCl_2$. The nmr (90 MHz) spectrum of chlorooxetane in CD_3CN showed a complex region between δ 4.4 and 5.1 ppm.

Treatment of chlorooxetane (neat) at 0° with anhydrous HCl gave 2,3-dichloropropanol in about 90% yield. The product was analyzed by gc and ir.

3-Oxetanone (from 3-Oxetanol).—Oxetanol (11.3 g, 0.153 mol) in methylene chloride (900 g) was treated at 20–25° with freshly prepared $CrO_3 \cdot 2C_5H_5N$ (225 g, 0.88 mol). After 30 min gc (125°, silicone column) showed complete conversion of oxetanol and the appearance of a new peak with a retention time of 1 min. The reaction mixture was filtered and the filtrate was flash distilled to remove dissolved chromium salts. Attempts to dry a portion of the solution with BaO resulted in disappearance of the new peak. Distillation through a 24-in. spinning band still gave a fraction (15.5 g) over the temperature range 88–115°. Gc analysis indicated the presence of mainly pyridine and 39% of the new peak. The latter peak was isolated by preparative gc and identified as 3-oxetanone [6.05 g (0.084 mol), 55% yield] by infrared and nmr: ir 5.47 (C=O) and 10.4 μ (oxetane ring); nmr (60 MHz, $CDCl_3$) singlet at δ 5.40 ppm. Carbonyl analysis using $NH_2OH \cdot HCl$ indicated a purity of >96%. Purified product had micro boiling point (Emich) 106°, d_4^{27} 1.137, and $n^{25}\mathrm{D}$ 1.4224. Redistillation through a 24-in. annular still (Nester-Faust) gave pure product.

Anal. Calcd for $C_3H_4O_2$: C, 50.0; H, 5.6. Found: C, 49.8; H, 5.6.

Polymerization of oxetanone occurred during storage at ambient temperature, giving a highly viscous material which showed infrared bands at 5.8 (C=O) and 9.0–9.5 μ (COC).

Oppenauer oxidation of 3-oxetanol did not yield 3-oxetanone. Acetone, cyclohexanone, quinone, anisaldehyde, and cinnamaldehyde were employed as hydrogen acceptors in conjunction with aluminum isopropoxide in benzene and xylene as solvents. Although acetone was obtained as overhead product, only trace quantities of oxetanone were observed by ir and gc.

3-Oxetanone (from Oxetyl Tosylate).—Oxetyl tosylate (3.7 g, 16 mmol), DMSO (10 ml), and tri-n-butylamine (5 ml) were heated to reflux in a 25-ml flask attached to a 6-in. Vigreux column and distillation head. A total of 2.7 g of foul-smelling distillate was obtained over a 30-min period. Gc (80°, silicone column) showed six components which were trapped and identified by mass spectral and ir analysis. The weight per cent composition was as follows: CH_3SH, 23%; CH_3SCH_3, 30%; butyraldehyde, 24%; 3-oxetanone, 14% (5.3 mmol, 33% yield); unknown, 2.5%; and CH_3SSCH_3, 7%. The butyraldehyde (9.0 mmol) may arise from oxidative decomposition of n-Bu_3N or by rearrangement and decomposition of the ionic intermediate

$$\overline{CH_2OCH_2C}HO\overset{+}{S}(CH_3)_2$$

Further work is needed to ascertain the origin of butyraldehyde.

3-Diethylaminooxetane.—3-Iodooxetane (5 ml, 57 mmol) and diethylamine (25 ml) were heated in a 100-ml Fischer–Porter aerosol compatibility tube for 1 hr at 200°. Extraction with petroleum ether (bp 30–60°) followed by filtration and atmospheric distillation (maximum temperature: flask 141°, head 62°), gave 9.6 g of a dark brown, crystalline solid and 6.7 g of liquid. Gc (150°, Carbowax column) and ir showed the presence of allyl alcohol (15.5 mmol), unreacted iodooxetane (3.8 mmol), a high boiler, and an intermediate peak with a slight amine-like odor which was identified as 3-diethylaminooxetane. Distillation through a 24-in. spinning band still gave diethylaminooxetane [1.61 g (12.5 mmol), 23% yield], bp 54° (5 mm), and 2.46 g of a higher boiling fraction, bp 60–65° (0.2 mm). Diethylaminooxetane showed ir bands at 7.25 (CH_3) and 10.25 μ (oxetane ring). A chromatographic cut had d_4^{26} 0.900, $n^{20}\mathrm{D}$ 1.4427, and neut equiv 127 (calculated 129). In the nmr (60 MHz, $CDCl_3$) four signals were observed in the ratio 3:2:1:4, δ_D 0.98 (CH_3, triplet), δ_C 2.48 (NCH_2, quartet, $J_{CD} = 6.9$ Hz), δ_B 3.82 (ring CH, second-order splitting observed), and δ_A 4.58 ppm (ring CH_2 groups, doublet, splitting 6.5 Hz).

Anal. Calcd for $C_7H_{15}ON$: C, 65.1; H, 11.7; N, 10.8. Found: C, 65.0; H, 11.6; N, 10.6.

The crystalline solid was recrystallized from benzene, mp 170–172°. It was identified as $(C_2H_5)_2NH \cdot HI$ by comparison of its ir spectrum with that of an authentic sample.

Anal. Calcd for $C_4H_{12}NI$: I, 62.2. Found: 62.0.

2,3-(Diethylamino)propanol.—The high-boiling fraction obtained in the distillation of diethylaminooxetane was identified by ir and nmr as 2,3-(diethylamino)propanol. Gc showed the fraction to be 76% pure [1.87 g (9.3 mmol), 17% yield]. A sample purified by preparative gc had d_4^{26} 0.877 and $n^{20}\mathrm{D}$ 1.4510; ir 2.91 (OH) and 7.22 μ (CH_3); nmr (60 MHz, $CDCl_3$) four signals were observed in the ratio 12:11:2:1, 1.03 (triplet, CH_3–), 2.2–3.2 (complex multiplet, NCH– and NCH_2–), 3.5–3.8 (complex multiplet, CH_2O), and 4.85 ppm (broad singlet, hydroxyl). After treatment with a chemical shift complexing reagent, $Eu[CF_3CH_2CF_2C(O)CHC(O)CH(CH_2)_3]_3$, the following spectrum was obtained: four signals were observed in the ratio 12:10:1:2, 1.21 and 1.29 (two triplets, CH_3–), 2.4–3.3 (complex multiplet, NCH_2), 3.87 (pentet, methine proton), and 4.86 ppm (doublet, OCH_2).

Anal. Calcd for $C_{11}H_{26}N_2O$: C, 65.29; H, 12.95; N, 13.85. Found: C, 65.48; H, 12.78; N, 13.68.

Dehydrochlorination of 3-Chlorooxetane.—Chlorooxetane (5.5 g, 58 mmol), powdered NaOH (4.6 g, 116 mmol), and diisobutylcarbinol (20.5 g) were heated to reflux in a 50-ml flask fitted with thermometer, 6-in. glass helices packed column, and distillation head. Six grams of distillate was obtained over the temperature range 80–110°. Gc (135°, Igepal column) and ir showed the presence of chlorooxetane (major) and small amounts of ethanol, propanol, and allyl alcohol as well as solvent.

Dehydroiodination of 3-Iodooxetane.—Sodium (5.8 g, 0.25 g-atom) was dissolved in 2,6,8-trimethyl-4-nonanol (140 g). The solution was cooled to 57° and iodooxetane (46 g, 0.75 mol) was added dropwise. The reaction mixture was distilled under reduced pressure; 34 g of distillate was obtained over the temperature range of 29 (35 Torr) to 72° (8 Torr). Gc (135°, Igepal column) and ir analysis showed the presence of ethanol, acrolein, propanol, unreacted iodooxetane, and some solvent.

Catalytic Dehydration of 3-Oxetanol over Alumina.—Oxetanol (5.5 g, 74 mmol) was added dropwise into a glass tubular reactor packed with Harshaw alumina (No. Al-0104, $^3/_{16}$ in.) and heated to 400° in a tube furnace. At a pressure of 100 Torr and a residence time of 0.5 to 1.0 sec, 3.3 g of starting material was collected in the ice trap and 1.7 g of reaction products was collected in the Dry Ice trap. Gc (70°, silicone column) and ir analysis of the reaction products showed the presence of water, formaldehyde, acetaldehyde, and acrolein.

Oxetyl Acetate.—3-Oxetanol (25.0 g, 0.338 mol), metallic sodium (0.4 g), and allyl acetate (200 ml) were heated to reflux in a 300-ml flask fitted with a 12-in. packed column and distillation head. Distillate (containing allyl alcohol) was slowly taken off while more allyl acetate was added to maintain a constant level in the flask. When the conversion had reached about 60% (gc analysis, 125°, silicone column) the excess allyl acetate was distilled and the residue was vacuum distilled, giving oxetyl acetate (18 g, 0.155 mol) and oxetanol (11 g, 0.15 mol). Corrected yield of oxetyl acetate was 83%; bp 76° (29 mm);

d_4^{30} 1.123 and n^{20}_{D} 1.4241; ir 5.73 (C=O), 8.13 (=COC), and 10.31 (oxetane ring).

Anal. Calcd for $C_5H_8O_3$: C, 51.7; H, 7.81. Found: C, 51.6; H, 7.92.

Oxetyl acetate was also prepared by acylation of oxetanol with acetyl chloride. Oxetanol (5.63 g, 76 mmol) in benzene (75 ml) containing Et_3N (7.70 g, 76 mmol) was treated at 0° with acetyl chloride (5.96 g, 76 mmol). After 30 min gc showed a conversion of 95%. The reaction mixture was extracted with 75 ml of water and the organic phase was washed three times with 10-ml portions of water. Analysis of the water extract after 2 days showed the presence of product, which was extracted with three 15-ml portions of benzene after saturation with salt. Some product was probably lost through hydrolysis in the aqueous phase. The combined organic layers were distilled at atmospheric pressure to remove solvent and the crude product was vacuum distilled through a 6-in. glass helices packed column to give oxetyl acetate (5.33 g, 46 mmol, 64% corrected yield), bp 46–47° (7 mm).

Oxetyl Acrylate.—3-Oxetanol (50.0 g, 0.68 mol), ethyl acrylate (134 g), aluminum isopropoxide (1.5 g), and phenyl-β-naphthylamine (3 g) were heated to reflux. Only a trace of ethanol was found in the distillate. Metallic sodium, (0.5 g) was added, and 100 ml of ethyl acrylate was distilled and replaced with 100 ml of allyl acrylate. The latter was slowly distilled and the residue was vacuum distilled, giving 3-oxetanol (34 g, 0.46 mol), a higher boiler [74–76° (1 Torr), 6 g], and 12 g of pot residue. The oxetanol fraction contained about 5% of a higher boiling material which was trapped by gc (125°, silicone column) and identified as oxetyl acrylate (6% yield) by ir.

Oxetyl acrylate was also prepared by reaction of oxetanol with acrylyl chloride. Oxetanol (5.63 g, 76 mmol) in benzene (75 ml) containing Et_3N (7.70 g, 76 mmol) was treated at 0° with acrylyl chloride (6.88 g, 76 mmol). Conversion after 30 min as determined by gc was about 95%. The reaction mixture was worked up as described under the preparation of oxetyl acetate. The distilled oxetyl acrylate [3.5 g, (27 mmol), 38% corrected yield] had the following physical properties: bp 58° (6.5 mm); d_4^{28} 1.111; n^{20}_{D} 1.4515; ir 5.81 (C=O), 6.13 and 6.18 (C=C), and 10.31 μ (oxetane ring).

Anal. Calcd for $C_6H_8O_3$: C, 56.2; H, 6.29. Found: C, 56.1; H, 6.14.

Ethyl 3-(3′-Oxetoxy)propionate.—The high-boiling fraction obtained in the preparation of oxetyl acrylate was identified by nmr as ethyl 3-(3′-oxetoxy)propionate (0.035 mol, 16% yield): d_4^{21} 1.090; n^{21}_{D} 1.4384; ir 5.77 (C=O), 8.45 (=COC), and 10.29 μ (oxetane ring).

Anal. Calcd for $C_8H_{14}O_4$: C, 55.2; H, 8.10. Found: C, 55.1; H, 8.03.

Attempted Dehydroacetoxylation of Oxetyl Acetate.—In the first experiment oxetyl acetate (9.3 g, 0.08 mol) was passed in 7 min through a 30 × 1 cm Vycor tube at 490 ± 10°. Almost all of the oxetyl acetate was recovered unchanged. In a second run oxetyl acetate (8.1 g, 0.07 mol) was passed in 40 min through the reactor at 605 ± 5°. The condensate was collected in pyridine (14 g) cooled to −40°. This receiver was followed by a water condenser and a −78° trap. The condensate in the first receiver amounted to 6.3 g; nothing was collected in the −78° trap. Gc (Igepal column) and ir showed a small amount of H_2O and unchanged starting material.

Oxetyl acetate was heated in a sealed tube with excess diethylamine for several hours at 150°; no evidence of reaction was observed.

Polyoxetanol.—A freshly distilled sample of 3-oxetanol (about 150 g) became hazy after several weeks under ambient conditions and after a few months it had a milky appearance. Filtration and ether washing gave 0.6 g of white, amorphous powder, mp 125–130°, mol wt (osmometric), 1397. The milky filtrate was distilled (65°, 5 Torr) and the pot residue was dissolved in hot ethanol. On cooling an additional 1.5 g of precipitated polyoxetanol was obtained, mp 125–135°, mol wt, 1723. Both fractions of polyoxetanol were water soluble, ir (KBr) 2.97 (OH) and 8.99 μ (COC), nmr (DMSO-d_6) doublet centered at 4.66 ppm (sec OH).

Anal. Calcd for $(C_3H_6O_2)_x$: C, 48.6; H, 8.16. Found: C, 47.8; H, 8.2.

Registry No.—**1,** 6777-00-0; *cis*-**2,** 40307-01-5; *trans*-**2,** 40307-02-6; **4,** 7748-36-9; **4** polymer, 39275-61-1; **11,** 26272-83-3; **12,** 26272-86-6; **13,** 39267-79-3; **14,** 26272-85-5; **15,** 39267-81-7; **16,** 6704-31-0; **18,** 39267-83-9; **19,** 39267-84-0; **20,** 39267-85-1; tosyl chloride, 98-59-9; diethylamine hydriodide, 19833-78-4; 2,3-(diethylamino)propanol, 13429-30-6; 3-chlorooxetane, 4741-80-4; allyl acetate, 591-87-7; acetyl chloride, 75-36-5; ethyl acrylate, 140-88-5; acrylyl chloride, 814-68-6.

Acknowledgment.—The authors are indebted to Dr. R. C. Rittner, Mr. J. Culmo, and Mr. J. Giunta for microanalyses, and to Mr. G. D. Vickers and Dr. T. Groom for nmr analyses.

On the Mechanism of Alkaline Hydrolysis of Methylthiopurines[1]

URI REICHMAN, FELIX BERGMAN,* DOV LICHTENBERG, AND ZOHAR NEIMAN

Department of Pharmacology, The Hebrew University–Hadassah Medical School, Jerusalem, Israel

Received January 16, 1973

Di- and trimethylthiopurines, which can form anions, are resistant to alkaline hydrolysis. After introduction of an *N*-methyl substituent, these compounds are incapable of forming anions and become susceptible to attack by hydroxyl ion. The course of these reactions can be predicted satisfactorily by Fukui's superdelocalizabilities for nucleophilic attack; the same order of reactivities is derived for analogous methylthio- and chloropurines, in accordance with the limited experimental observations.

Many attempts have been made to establish the order of reactivity of purines toward nucleophilic reagents. The most useful model is 2,6,8-trichloropurine (TCP), in which nucleophilic displacement of the halogens by a variety of bases follows the order 6 > 2 > 8.[2-4] However, for 7- and 9-methyl-TCP, the relative reactivity toward ethoxide ion was found to be 8 > 6 > 2.[4,5] The latter result is in good agreement with the observations of Barlin[6] on the three isomeric 9-methylmonochloropurines and has been explained as follows.[5] The reaction of TCP with bases involves the anion of the substrate, in which the negative charge is concentrated mainly in the imidazole ring, thus making nucleophilic attack at C-8 difficult. The 7- or 9-methyl derivatives of TCP cannot form anions and thus follow the order of reactivity derived

(1) Dedicated to our teacher and friend, Professor E. Lederer, Director, Institut de Chimie des Substances Naturelles, Gif-Sur-Yvette, France, on the occasion of his 65th birthday.

(2) (a) E. Fischer, *Chem. Ber.*, **30**, 2226 (1897); (b) R. K. Robins and B. E. Christensen, *J. Amer. Chem. Soc.*, **74**, 3624 (1952).

(3) S. R. Breshears, S. S. Wang, S. G. Bechtolt, and B. E. Christensen, *J. Amer. Chem. Soc.*, **81**, 3789 (1959).

(4) E. Fischer, *Chem. Ber.*, **30**, 1846 (1897).

(5) E. Y. Sutcliffe and R. K. Robins, *J. Org. Chem.*, **28**, 1662 (1963).

(6) G. B. Barlin, *J. Chem. Soc. B*, 954 (1967).